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EXAMINER

KUBELIK, ANNE R

ART UNIT

PAPER NUMBER

1638

21

DATE MAILED: 06/02/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/411,863

Applicant(s)

IZHAR, SHAMAY

Examiner

Anne R. Kubelik

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 20 March 2003.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 47,49,51 and 55-79 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 47,49,51 and 55-79 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 05 June 2001 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
* See the attached detailed Office action for a list of the certified copies not received.
- 14) ☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892) 4) ☐ Interview Summary (PTO-413) Paper No(s). _____
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948) 5) ☐ Notice of Informal Patent Application (PTO-152)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ 6) ☐ Other: _____

DETAILED ACTION

1. The claims have been amended, cancelled or added as requested in Paper No. 20, filed 20 March 2003. Claims 47, 49, 51 and 55-79 are pending.
2. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Response to Amendment

3. The objection to claim 55 is obviated by its cancellation.
4. The rejections of claim 55 under 35 U.S.C. 112, first paragraph, for new matter and under 35 U.S.C. 102(b) as being anticipated by Fabijanski et al are obviated by its cancellation.

Claim Objections

5. Claims 59 and 61 are objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. Parent claims 58 and 60 state that the plant is characterized by exogenic allelism, which the specification states is the "allellic positioning of two functionally distinct exogenes on the chromosomes of a chromosome pair such that substantially 100% segregation of the two exogenes is observed upon gamete formation" (paragraph spanning pg 26-27). Thus, claims 59-61 fail to further limit claims 58 and 60, respectively.
6. Claims 59, 61, 64 and 73 are objected to because of the following informalities:

In claims 59 and 61, commas should be inserted after “exogenes” and “relationship”.

An article is missing before the first “RNA” in claims 64 and 73, line 2.

Claim Rejections - 35 USC § 112

7. Claims 47, 49, 51 and 55-79 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter that was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. The rejection is modified from the rejection set forth in the Office action mailed 22 October 2002, as applied to claims 47, 49 and 56-57. Applicant’s arguments and the Declaration of Dr. Vered Yesodi, both filed 20 March 2003, have been fully considered but they are not persuasive.

The claims are drawn a method of generating exogenic allelism, wherein one step of the method comprises introducing a recombinase into a plant by topical application. The claims are also drawn to the method wherein the exogenes are RNA molecules or encode a transactivator that is non-operable with eukaryotic promoters. Lastly, the claims are drawn to a method of generating exogenic allelism, wherein the alleles encode any gene.

However, the specification does not teach introduction of a recombinase into a plant by topical application. The specification only teaches introduction of a recombinase into the plant by crossing with a plant transformed with a nucleic acid encoding a recombinase.

The specification also does not teach transformation of a plant with a RNA molecule or a transactivator that is non-operable with eukaryotic promoters. There is no known transactivator

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that would not be expressed from a eukaryotic promoter. Transformation with RNA would not result in integration of the exogene into the plant.

Lastly, the specification does not teach gene combinations suitable for exogenic allelism other than those involved in making male sterile plants. As the purpose of the method appears to be making plants where the two genes segregate in the progeny, it is unclear what genes other than those involved in conferring male sterility it would be desirable to have in the plant. The specification does not teach other such genes.

Applicant urges that it was never the intention of Applicant to attempt to topically apply the recombinase protein to the plant but rather, as taught in the specification and explained in the Powerpoint presentation (part of the Declaration) that recombinase can be introduced by crossing with plants known to carry an active recombinase. Furthermore, in light of this, Applicant sees no contradiction between the teachings of Gidoni et al, who state that germinal transmission of the recombined loci is required, and Applicant's use of the recombinase (response pg 7-8).

This is not found persuasive because the method reads on topical application of the recombinase. The method does not recite, for example, introducing into the first plant a nucleic acid encoding a recombinase or crossing the first plant with a plant that has been transformed with a nucleic acid encoding a recombinase. Topical application of the recombinase is not enabled.

Lastly, the claims are drawn to a method step of introducing a recombinase into a plant. The instant specification fails to provide guidance for topical application of a recombinase protein to a plant, for getting the applied protein into the plant, and for having it reliably result in specific recombination. The instant specification only provides guidance for introduction into a

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plant of a nucleic acid encoding a recombinase. In the response filed 7 August, 2002, Applicant did not provide an explanation for how topical application of the recombinase is enabled by the specification.

Applicant urges that the Declaration of Dr. Vered Yesodi and Powerpoint presentation provides evidence of enablement, and as Dr. Vered Yesodi has declared as one of skill in the art that the specification is enabled, and provided a presentation explaining the method, the invention would be enabled (response pg 8).

The remainder of the enablement rejection presented in previous Office actions, is withdrawn in light of the Declaration of Dr. Vered Yesodi.

8. Claims 47, 49, 51 and 55-79 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter that was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The rejection is modified from the rejection set forth in the Office action mailed 22 October 2002, as applied to claims 47, 49, 50-51, 55 and 56-57, due to amendment. Applicant's arguments and the Declaration of Dr. Vered Yesodi, both filed 20 March 2003, have been fully considered but they are not persuasive.

The specification does not describe transactivators non-operable with eukaryotic promoters, and it is entirely unclear what these might be.

Applicant urges that the examiner has not met the burden of rebutting the presumption of written description. Applicant urges that the invention is directed to a method, not to specific nucleotide or peptide sequences. Applicant urges that each method step is described. Applicant also urges that the structural feature that distinguishes the claimed methods and plants is the

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production of plants having stable exogenic allelism, and this feature demonstrates possession (response pg 9).

This is not found persuasive. For a method to be described, the compositions used in the method must also be described. Because the exogenes are not described, the method is not. As for the plants, their phenotype is not described; thus, the plants are not described.

Applicant urges that their invention is not dependent upon the actual exogene used, and never intended their method only to be used with the exogenes of Figures 1 and 2. Applicant urges that the claims are drawn to methods and that the structural feature is the placement of the exogenes in stable allelic alignment. Applicant urges that the invention is not dependent upon the actual exogene chosen; that is to be done by the user. Furthermore, Applicant urges the Lastly, Applicant that in the Declaration of Dr. Vered Yesodi she states that she, as one of skill in the art, would understand that the inventor had possession of the invention at the time of filing. (response pg 9-11).

This is not found persuasive because the specification does not describe gene combinations suitable for exogenic allelism other than those involved in making male sterile plants. As the purpose of the method appears to be making plants where the two genes segregate in the progeny, it is unclear what genes other than those involved in conferring male sterility the inventor envisioned as being used in the invention. Thus, the description is lacking for the full breadth of the claimed invention.

9. Claims 47, 49 and 56-79 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter that Applicant regards as the invention. Dependent claims are included in all rejections.

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The following rejections are new, due to amendment of the claims.

Claim 47, part (c), and claim 49, parts (b) and (c), are indefinite in their recitation of “having the expression cassette wherein the third segment has been excised”. It is unclear what the phrase is intended to modify - the recombinase? The progeny? By position in the claims, the phrase modifies “recombinase”, but recombinases do not have expression cassettes.

Claims 58 and 60 are indefinite in their recitation of “characterized by exogenic allelism. It is unclear what the phrase is intended to modify - the method? The plant or seed? By position in the claims, the phrase modifies the method. Thus, it would appear that the claims do not further limit the parent claims, because the methods are ones of generating exogenic allelism. If Applicant intended that the phrase modify the plant or seed, it is suggested that --, wherein the plant or seed is-- be inserted after “47” or “49”, as appropriate.

Claims 64 and 73 are indefinite in their recitation of “wherein the first exogene is RNA molecule”. Genes transformed into plants are not generally RNA molecules. Did Applicant intend to indicate that the exogene encodes an RNA molecule?

Claims 65 and 74 are indefinite in their recitation of “transactivator non-operable with eukaryotic promoters”. It is unclear what Applicant intends. There is no known gene that is not operable with eukaryotic promoters.

Claim Rejections - 35 USC § 102

10. Claims 58-59 are rejected under 35 U.S.C. 102(e) as being clearly anticipated by Gutterson et al (US Patent 6,392,119, filed January, 1997). The rejection is repeated for the reasons of record as set forth in the Office action mailed 22 October 2002, as applied to claims

47, 50 and 55-56. Applicant's arguments filed 20 March 2003 have been fully considered but they are not persuasive.

Applicant urges that Gutterson et al fails to teach the step of selfing a plant resulting from step (b) and selecting a progeny devoid of recombinase having the expression cassette with the third segment excised (response pg 11).

This is not found persuasive because the plants produced by Gutterson et al would be identical to the instantly claimed plants (see Fig. 1).

Claim Rejections - 35 USC § 103

11. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

12. Claims 47, 56, 58-59 and 62-70 are rejected under 35 U.S.C. 103(a) as being unpatentable over Gutterson et al (US Patent 6,392,119, filed January, 1997).

The claims are drawn to a method of generating exogenic allelism comprising crossing a plant comprising a construct comprising a first promoter, a first transcribable nucleic acid, and between the two a second transcribable nucleic acid operably linked to a second promoter, flanked by site-specific recombination sequences, to a plant comprising a nucleic acid encoding a recombinase to generate progeny in which the first promoter and the first transcribable nucleic acid are operably joined, selfing the progeny plant, selecting a selfed progeny that lacks the

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recombinase to produce a plant wherein the expression cassette has the third segment excised, and backcrossing the selfed progeny to the first plant to generate progeny with exogenic allelism.

Gutterson et al teach a method of generating exogenic allelism comprising crossing a plant comprising a construct comprising a first promoter, a first transcribable nucleic acid, and between the two a second transcribable nucleic acid operably linked to a second promoter, flanked by site-specific recombination sequences, to a plant comprising a nucleic acid encoding a recombinase to generate progeny in which the first promoter and the first transcribable nucleic acid are operably joined, selfing the progeny plant (column 9, lines 48-50) to produce a plant wherein the expression cassette has the third segment excised (column 9, lines 44-48), and backcrossing the selfed progeny to the first plant to generate progeny with exogenic allelism (Fig. 1 and column 8, line 59, to column 10, line 7). The method is described in which the progeny plants are male sterile and female fertile (see Fig. 1). Gutterson et al also teach that the exogenes are to encode proteins that include barnase and ribonuclease T1, or RNAs like anti-sense RNAs and ribozymes (column 14, lines 21-39). The transactivator would be "non-operable with eukaryotic promoters".

Gutterson et al do not disclose selecting a selfed progeny that lacks the recombinase.

At the time the invention was made, it would have been obvious to one of ordinary skill in the art to modify the method of generating exogenic allelism as taught by Gutterson et al, to select a selfed progeny that lacks the recombinase. One of ordinary skill in the art would have been motivated to do so because one of skill in the art would know that the presence of the recombinase in the selfed progeny would mean that when the selfed progeny is backcrossed to

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the first plant, the resulting progeny would be subject to the action of the recombinase and progeny with exogenic allelism would not be produced.

13. Claims 49, 51, 57, 60-61, and 71-79 are free of the prior art, given the failure of the prior art to teach a method of backcrossing plants produced by a recombination system in which the plants have the construct described in claim 49.

Conclusion

14. No claim is allowed.

15. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Anne R. Kubelik, whose telephone number is (703) 308-5059. The examiner can normally be reached Monday through Friday, 8:30 am - 5:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Amy Nelson, can be reached at (703) 306-3218. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 872-9306 for regular communications and (703) 872-9307 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to Customer Service at (703) 308-0198.

Anne R. Kubelik, Ph.D.
May 21, 2003

A handwritten signature in black ink, appearing to read "Amy Nelson", with a stylized flourish at the end.

AMY J. NELSON, PH.D
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